DIAGNOSTIC VALUE OF INDICES OF BRONCHIAL HYPERRESPONSIVENESS FOR A VERIFICATION OF EOSINOPHILIC ASTHMA PHENOTYPE IN CHILDREN UNDER THE POLYMORPHISM OF N-ACETYLTRANSFERASES

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ДІАГНОСТИЧНА ЦІННІСТЬ ПОКАЗНИКІВ БРОНХІАЛЬНОЇ ГІПЕРРЕАКТИВНОСТІ У ВЕРИФІКАЦІЇ ЕОЗИНОФІЛЬНОГО ФЕНОТИПУ БРОНХІАЛЬНОЇ АСТМИ У ДІТЕЙ ІЗ УРАХУВАННЯМ ПОЛІМОРФІЗМУ N-АЦЕТИЛТРАНСФЕРАЗ

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Introduction. Bronchial asthma (BA) in children is considered as one of the most common chronic diseases, which is not showing a tendency to decrease all over the world, despite scientific advances, explaining the nature of the disease. the prevalence of asthma varies in different countries and populations and ranged from 1 % to 18 %, but in the children population this index ranges 5 %–10 % depending on age and sex characteristics [1].

Bronchial asthma is a classic multifactorial disease, in which development an important role plays environmental factors as well as genetic predisposition to the development of this pathology [2]. Phenotype heterogeneity of the disease is determining by the numerous differences in etiological factors, the types of the airway inflammation, the severity of bronchial hyperresponsiveness and by different genetic markers [1, 3, 4]. However, the fact that the genetic factor is a one of significant components playing role in asthma control achievement remains the undisputed, because it forms a specific phenotype of bronchial asthma and, as well, causes both features of responses to stimuli of the environment and response to drug therapy [2].

Considering literature data about the association of allergic asthma with genetically determined polymorphism of N-acetyltransferases, which determines the features of metabolic processes [5], it seemed important to assess the relationship of type of acetylation with bronchial hyperreactivity, which is also considered to be genetically inherited characteristic.

The aim of research. To estimate the diagnostic value of indices of bronchial hyperresponsiveness for a verification of eosinophilic asthma phenotype in children taking into account the polymorphism of the N-acetyltransferase genes.

Materials and methods. At the Chernovtsy Regional Children's Clinical Hospital 116 school-age children with persistent bronchial asthma have been examined. A cytological analysis of induced by inhalation of hypertonic solutions (3 %, 5 %, 7 %) of sodium chloride, sputum has been performed to all patients by the method of Pavord I.D. in the modification of Pizzichini M.M. (1996). The eosinophilic phenotype of BA was identified in patients who had 3 % or more of eosinophils in induced sputum. But noneosinophilic (neutrophilic) asthma phenotype was verified in school-aged children under the presence of the total number of eosinophils 2 % and less in cells sediment of sputum [3].

Type of acetylation has been determined by the method of Prebstyng and Gavrilov in modification of Timofeeva (1971). Airway hyperreactivity (AHR) was determined according to the «dose-response curve» (DRS), which reflects the steepness of slope of the «flow-volume» curve during inhalation histamine challenge test. The obtained data have been interpreted taking into account the fact that the higher the HRB is associating to the higher DRS (calculated in conventional units) [4].

These survey results were analyzed by the methods of biostatistics and clinical epidemiology, and using the software package STATISTICA 5.0 Stat Soft Inc. and Excel XP for Windows on a PC, by parametric (Student's t criterion) and nonparametric (Fisher φ criterion) methods of calculation and by methods of biostatistics and clinical epidemiology with the evaluation of statistic values of diagnostic tests: specificity (Sp), sensitivity (Se), positive and negative predictive values (PPV and NPV respectively) with estimation of their 95 % confidence intervals (95 % CI), as well as likelihood ratio for positive (LR+) and for negative (LR–) test results.

Results and Discussions. To the first (I-st) clinical group 66 children (56,9 %) with eosinophilic phenotype of BA were referred, but second (II-nd) comparison group was formed by 50 patients (43,1 %) with neutrophilic asthma phenotype. The groups of comparison were comparable by the main clinical characteristics (sex, age, place of residence).

It has been stated that among patients with eosinophilic BA the slow type of acetylation was recorded more often. Thus, in the I-st group a content in urine of acetylated sulfadimezin less than 75 %, which is associated with slow acetylating type, has been determined in half of the patients (50,0±7,2 %), but only in one third of patients (35,9 ± 7,6 %) of the comparison group ($P > 0,05$).

Assessing the results of histamine provocative test it has been found that a significantly higher AHR was determined in patients with eosinophilic asthma phenotype. Thus, a geometric mean of DRS was 2,1 ± 0,1 in children of I-st clinical group, but 1,8 ± 0,1 in patients of the comparison group ($P < 0,05$).

At the same time, in a cohort of patients with the significant bronchial reactivity, which was determined by the level of DRS ≥ 1,8, a slow acetylating type has been recorded twice as often in school-age children with eosinophilic asthma phenotype. Thus, in a population of children with the above AHR, the quota of patients with slow type of acetylation was 55,0 % in the I-st clinical group and only 25,0 % in the comparison group ($P\varphi < 0,05$).

At that, the presence of significant airway hyperresponsiveness to histamine (RDS ≥ 1,8) under the simultaneous recording of slow acetylating type in children with BA, can only be used as an additional diagnostic test confirming eosinophilic asthma phenotype (Sp = 76 % [95 % CI 61,8–86,9], PPV = 75 % [95 % CI 60,4–86,4]), but not as an independent screening marker, in view of the registration of false-negative results of this integrated test in a third (28 %) patients (Se = 72 %, NPV = 73 %), as well as due to the low likelihood ratios of this test results for a verification of the disease (LR+ = 3,0 and LR– = 0,4).

Conclusions. Thus, the most significant increase of bronchial hyperreactivity has been detected in bronchial asthma school-age patients with eosinophilic type of airway inflammation, especially under association with a slow acetylating type. However, in asthmatic children the presence of significant airway hyperresponsiveness to histamine (DRS ≥ 1,8), associated with a slow type of acetylation can only be used as an additional diagnostic test confirming eosinophilic bronchial asthma, but not as an independent screening marker of this asthma phenotype.

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БУДУЩИЕ ВРАЧИ КАК ГРУППА РИСКА ПО ИНФИЦИРОВАНИЮ ВИРУСОМ ИММУНОДЕФИЦИТА ЧЕЛОВЕКА

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Медицинский персонал лечебно-профилактических учреждений является группой профессионального риска по инфекционным заболеваниям, в том числе, по гемоконтактным инфекциям. Студент-медик должен грамотно оценивать степень риска инфицирования при выборе своей будущей специальности. В 2013 году было проведено анонимное анкетирование среди студентов Южно-Уральского государственного медицинского университета с целью выявления их информированности о некоторых аспектах заражения вирусом иммунодефицита человека.